FINAL ACTION

Applicant's amendment of 7-27-10 has been fully considered. Applicant's argument has not overcome the previous rejections of 112/2nd, and 103 based on **Baxter et. al.** (US'005).

Claims 1, 2, 8, 9, 12-27, 29, 32, 35, 38, 40-49, 51-83 and 102-105 are cancelled.

Claims 84-98 are withdrawn.

Claims 3-7, 10, 11, 28, 30, 31, 33, 34, 36, 37, 39, 50 and 99-102 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 5 remains rejected under 35 U.S.C. 112, second paragraph, for lacking antecedent basis because claim 5 recites the limitation "*ethyl*" or "*methylamide*" in the majority of the species recited. There is insufficient antecedent basis for this limitation in the claim.

Only the first three species of claim 5 belong to the subgenus of formula III, the rest of the species recited does not fall within the scope of formula III because they have an "*ethyl*" linkage at the 2-position, and a *methylamide* group.

2. Claims 7, 11 and 101 remain rejected under 35 U.S.C. 112, second paragraph, for lacking antecedent basis because claims 7, 11 and 101 recite the limitation "*ethyl*" or "*methylamide*" in the majority of the species recited. There is insufficient antecedent basis for this limitation in the claim.

In claim 7, the species that do not fall within the scope of formula III are:

a. the first four species on page 10,

b. the first 12 species on page 12,

c. the first, fifth and sixth species on page 13,

d. the 10th species on page 14,

e. the fifth thru the 15th species on page 15,

f. all species on pages 16 & 17,

g. the first four species on page 18.

All species in claims 11 and 101 do not fall within the scope of formula III.

Applicants' drawings of the structures are appreciated. As can be seen from such drawings, there is **no** ethyl group. If applicants intended to count the group "-CH-CH_3" as an "ethyl" group, then, where would the extra methyl group in "4,N-dimethyl..." be?

3. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "ethyl" in the species recited in claims 5, 7, 11 and 101 is used by the claim to mean "-CH-", while the accepted meaning is "-CH_2-CH_3." The term is indefinite because the specification does not clearly redefine the term.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

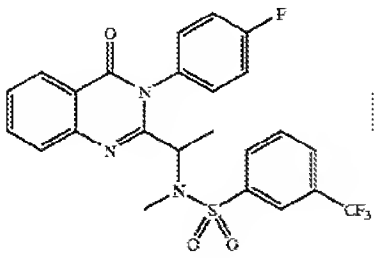
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

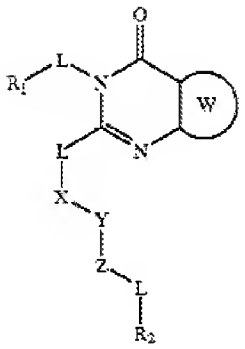
4. Claims 3-7, 10, 28, 30, 31, 33, 34, 36, 37, 39, 50 and 99 and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Baxter et. al.** (US'005 cited previously). The rejection is reiterated herein.

Claim 3 has been amended to exclude compound #14, which has the following structure:



Thus, the 102 rejection has been rendered moot. However, the reference provides a generic formula II that still encompasses the instant formula III when the disclosed formula II (in column 30) has the following structure and substituents:

Formula II



i. R_1 is an aryl group (or a phenyl group corresponding to the instant phenyl-$(R^{1a})_n$);

ii. R_2 is an alkyl or aryl group (or a phenyl group corresponding to the instant

iii. phenyl-$(R^{5a})_t$);

iv. L is absent or $-(CH_2)_nNR_2(CH_2)_p-$ (corresponding to the instant $-C(R^2,R^6)-N(R^4)-$);

v. n = 1; p= 0;

vi. X is a direct bond;

vii. Y is $-S(O_2)-$; Z is a direct bond;

viii. W is substituted or unsubstituted aryl fused to the pyrimidone ring (which provides the quinazolinone as seen in compound #14).

Although the reference does not disclose additional species of a sulfonamide substituent at the 2-position, the subgenus formula II in column 30 provides equivalency teaching for one skilled in the art to select compounds of the instant formula III to agonize or antagonize hedgehog pathway.

As admitted by applicant, the instant formula III is **encompassed** by the reference's formula II. Although no substituent is identified for R_1, R_2 and W, such a detail is not critical because the phenyl groups and R_3 of the instant formula III do not have to be substituted since **m, n and t can have a value of 0**. Besides, the preferred embodiment on column 32 presents a narrower subgenus that is closer to the instant formula III, and the definition for "aryl" and its substituents can be found in the last paragraph on column 23, see the following excerpt:

> The term "aryl" as used herein includes 5-, 6-, and 7-membered single-ring aromatic groups that may include from zero to four heteroatoms, for example, benzene, pyrrole, furan, thiophene, imidazole, oxazole, thiazole, triazole, pyrazole, pyridine, pyrazine, pyridazine and pyrimidine, and the like. Those aryl groups having heteroatoms in the ring structure may also be referred to as "aryl heterocycles" or "heteroaromatics." The aromatic ring can be substituted at one or more ring positions with such substituents as described above, for example, halogen, azide, alkyl, aralkyl, alkenyl, alkynyl, cycloalkyl, hydroxyl, alkoxyl, amino, nitro, sulfhydryl, imino, amido, phosphate, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether,

The disclosed formula II compounds are antagonists of hedgehog pathway, and thus, one skilled in the art would have been motivated to select the claimed compounds because such compounds could have had the same antagonistic effect. The reference does not have to disclose

the same utility to render obvious structurally similar compounds. Thus, applicant's argument of "No utility or even potential utility was disclosed or suggested for Baxter compounds … for use as quinazolinone modulators of nuclear receptors in general and (FXR) in particular, ... " is a moot point. See ***In re Dillon*** 919 F. 2d. 688, 693; 16 USPQ 2d. 1897, 1902 (Fed. Cir. 1990) regarding a prima facie case of obviousness of structurally similar compounds disclosed by a prior art regardless of the properties disclosed in the inventor's application.

Thus, it is maintained that compounds of the instant formula III are obvious over the reference's formula II as pointed out above.

Response to Applicants' argument: Applicants refuted the rejection on the ground that "a species cannot be patentable over a prior art genus", and cited several case laws to support the rebuttal.

The first cited chemical case law was *Integra Lifescience I, Ltd. v. Merck KGaA*, which did **not address** the issue of obviousness based on a reference's genus. The significance of said case law was about the section 35 U.S.C. 271(e)(1) which was interpreted as not providing a "safe harbor" for an infringement. The decision in said case law clarified that 35 U.S.C. 271(e)(1) allowed uses of a patented invention for the "development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." Thus, such a citation is irrelevant to the present 103 rejection.

The next cited case law was *Eli Lilly & Co. v. Board of Regents of the University of Washington*, which also did not address the issue of obviousness at all. The decision in said case affirmed the board on the finding of "no interference-in-fact" between Lilly's reissue application

and US'624 due to different sequences or chemical structures. Thus, said citation is also irrelevant.

In the case of *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.* the court ruled that the mere statement of "pretreatment regimens" in Kris et. al. would not be sufficient to render a method of premedicating with specific classes of drugs. However, in the instant case, the teaching of **Baxter et. al.** provided **more than** just a statement. It provides a subgenus of formula II (see column 30 of US'005) that is structurally similar to the instant formula III. It also disclosed compound #14 that exemplified what other quinazolinone sulfonamide compounds contemplated by Baxter. **The motivation for selecting compounds of the instant formula III would come from modifying compound #14 of Baxter et. al. with substituents listed for formula II.** Thus, the teaching of **Baxter et. al.** cannot be equated to that of Kris et. al. which only speculated a general regimen.

In the case of *In re Jones (958 F. 2d 347,350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992))*, the court ruled that there was no prima facie case of obviousness because the claimed salt has a structure different from the reference's salt even though both are amine salts. "The claimed salt is a primary amine with an ether linkage. The diethanolamino salt disclosed by Richter is a secondary amine, without an ether linkage." The "ether linkage" in the claimed salt imparted patentability on the structure of the claimed salt. Thus, the issue in *In re Jones* was not simply a question of a genus rendered obvious a species. It was more of structural homologs which was not found in the list of amine salts provided by the reference (Richter). Again, the scenario is

not the same as the **equivalent teaching provided by Baxter et. al.** where an exemplified compound was also disclosed. Thus, *In re Jones* is not applicable.

In the case of *In re Baird*, there was no exemplified compound in the teaching of Knapp et. al. Thus, it could not be used to support applicant's position to refute the 103 rejection based on Baxter et. al. Note, at the end of *In re Baird*, the court cited a quote from *In re Burckel*, 592 F. 2d 1175, 1179, 201 USPQ 67, 70 (CCPA1979): "[A] reference must be considered not only for what it expressly teaches, but also for what it fairly suggests." In the instant case, Baxter et. al. not only provided an equivalent teaching, but also provided an exemplified compound, which would give sufficient motivation for one skilled in the art to select and make compounds of the instant formula III.

In all consideration, the Baxter's teaching still renders obvious compounds of the instant formula III.

Claim Objections

4. Claim 100 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 100 recites a pharmaceutical composition with an additional antihyperlipidemic agent which is not taught or fairly suggested by the prior art of record.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on Monday thru Friday (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tamthom N. Truong
Examiner
Art Unit 1624

***

10-20-10